

Status of the Joint NICEATM/ECVAM Validation Study

NICEATM and the European Committee on the Validation of Alternative Methods (ECVAM) are conducting a collaborative validation study to evaluate the usefulness of two in vitro basal cytotoxicity assays proposed for predicting starting doses for in vivo acute oral toxicity assays and lethal concentrations in humans. Expert scientists recommended the study during an earlier ICCVAM International Workshop on *In Vitro* Methods for Assessing Acute Systemic Toxicity. Three laboratories are participating in the evaluation of the neutral red uptake assay using both a mouse cell line (i.e., BALB/c 3T3 fibroblasts) and a primary human cell type (i.e., normal human epithelial keratinocytes). The cytotoxicity results for the 72 coded chemicals to be tested, representing a wide range of toxicity, will be used to predict starting doses for in vivo acute oral lethality assays. Simulation modeling of animal use for acute oral toxicity testing by the Up-and-Down Procedure will determine the number of animals saved by using the predicted starting dose. Phase Ia cytotoxicity testing, completed in November 2002, established acceptable positive control ranges for each laboratory. Phase Ib testing of three coded chemicals, completed in May 2003, yielded changes in the protocols to further improve interlaboratory reproducibility. Phase II testing of 9 coded chemicals was completed in November 2003. The labs are currently using the final optimized Phase III protocols to test 60 chemicals. Testing is expected to be completed by the end of 2004.

Updated: August 9, 2004